

THE **WORLD'S** **GREATEST** **LIBRARY**

3690	3700	3710	3720	3730	3740	3750
* * *	* * *	* * *	* * *	* * *	* * *	* * *

FIGURE 1D

```

AAAAAAAAA AAAAAAAAAAG AATTCCTGCA GCCCGGGGGA TCCACTAGTT CTAGAGGGCC CGTTTAAACC
      3760      3770      3780      3790      3800      3810      3820
      *      *      *      *      *      *      *
CGCTGATCAG CCTCGACTGT GCCTTCTAGT TGCCAGCCAT CTGTTGTTTG CCCCTCCCCC GTGCCTTCCT

      3830      3840      3850      3860      3870      3880      3890
      *      *      *      *      *      *      *
TGACCCTGGA AGGTGCCACT CCCACTGTCC TTCCCTAATA AAATGAGGAA ATTGCATCGC ATTGTCTGAG

      3900      3910      3920      3930      3940      3950      3960
      *      *      *      *      *      *      *
TAGGTGTCAT TCTATTCTGG GGGGTGGGGT GGGGCAGGAC AGCAAGGGGG AGGATTGGGA AGACAATAGC

      3970      3980      3990      4000      4010      4020      4030
      *      *      *      *      *      *      *
AGGCATGCTG GGGATGCGGT GGGCTCTATG GCTTCTGAGG CGGAAAGAAC CAGCTGGGGC TCGAGAGCTT

      4040      4050      4060      4070      4080      4090      4100
      *      *      *      *      *      *      *
GGCGTAATCA TGGTCATAGC TGTTCCTGT GTGAAATTGT TATCCGCTCA CAATTCCACA CAACATACGA

      4110      4120      4130      4140      4150      4160      4170
      *      *      *      *      *      *      *
GCCGGAAGCA TAAAGTGTAAGCCTGGGGT GCCTAATGAG TGAGCTAACT CACATTAATT GCGTTGCCCT

      4180      4190      4200      4210      4220      4230      4240
      *      *      *      *      *      *      *
CACTGCCCGC TTTCCAGTCG GGAAACCTGT CGTGCCAGCT GCATTAATGA ATCGGCCAAC GCGCGGGGAG

      4250      4260      4270      4280      4290      4300      4310
      *      *      *      *      *      *      *
AGGCGGTTTG CGTATTGGGC GCTCTTCCGC TTCTCGCTC ACTGACTCGC TCGCTCGGT CGTTCGCTG

      4320      4330      4340      4350      4360      4370      4380
      *      *      *      *      *      *      *
CGGCGAGCGG TATCAGCTCA CTCAAAGCG GTAATACGGT TATCCACAGA ATCAGGGGAT AACGCAGGAA

      4390      4400      4410      4420      4430      4440      4450
      *      *      *      *      *      *      *
AGAACATGTG AGCAAAAGGC CAGCAAAAGG CCAGGAACCG TAAAAAGGCC GCGTTGCTGG CGTTTTTCCA

      4460      4470      4480      4490      4500      4510      4520
      *      *      *      *      *      *      *
TAGGCTCCGC CCCCTGACG AGCATCACAA AAATCGACGC TCAAGTCAGA GGTGGCGAAA CCCGACAGGA

      4530      4540      4550      4560      4570      4580      4590
      *      *      *      *      *      *      *
CTATAAAGAT ACCAGGCGTT TCCCCCTGGA AGCTCCCTCG TCGCTCTCC TGTTCCGACC CTGCCGCTTA

      4600      4610      4620      4630      4640      4650      4660
      *      *      *      *      *      *      *
CCGGATACCT GTCCGCCTTT CTCCCTTCGG GAAGCGTGCC GCTTTCTCAA TGCTCAGCT GTAGGTATCT

      4670      4680      4690      4700      4710      4720      4730
      *      *      *      *      *      *      *
CAGTTCGGTG TAGGTCGTTT GCTCCAAGCT GGGCTGTGTG CACGAACCCC CCGTTCAGCC CGACCGCTGC

      4740      4750      4760      4770      4780      4790      4800
      *      *      *      *      *      *      *
GCCTTATCCG GTAACATCG TCTTGAGTCC AACCCGGTAA GACACGACTT ATCGCCACTG GCAGCAGCCA

```

FIGURE 1E

4810	4820	4830	4840	4850	4860	4870
* * *	* * *	* * *	* * *	* * *	* * *	* * *
CTGGTAACAG	GATTAGCAGA	GCGAGGTATG	TAGGCGGTGC	TACAGAGTTC	TTGAAGTGGT	GGCCTAACTA
4880	4890	4900	4910	4920	4930	4940
* * *	* * *	* * *	* * *	* * *	* * *	* * *
CGGCTACACT	AGAAGGACAG	TATTTGGTAT	CTGCGCTCTG	CTGAAGCCAG	TTACCTTCGG	AAAAAGAGTT
4950	4960	4970	4980	4990	5000	5010
* * *	* * *	* * *	* * *	* * *	* * *	* * *
GGTAGCTCTT	GATCCGGCAA	ACAAACCACC	GCTGGTAGCG	GTGGTTTTTT	TGTTTGCAAG	CAGCAGATTA
5020	5030	5040	5050	5060	5070	5080
* * *	* * *	* * *	* * *	* * *	* * *	* * *
CGCGCAGAAA	AAAAGGATCT	CAAGAAGATC	CTTTGATCTT	TTCTACGGGG	TCTGACGCTC	AGTGGAACGA
5090	5100	5110	5120	5130	5140	5150
* * *	* * *	* * *	* * *	* * *	* * *	* * *
AAACTCACGT	TAAGGGATTT	TGGTCATGAG	ATTATCAAAA	AGGATCTTCA	CCTAGATCCT	TTTAAATTAA
5160	5170	5180	5190	5200	5210	5220
* * *	* * *	* * *	* * *	* * *	* * *	* * *
AAATGAAGTT	TTAAATCAAT	CTAAAGTATA	TATGAGTAAA	CTTGGTCTGA	CAGTTACCAA	TGCTTAATCA
5230	5240	5250	5260	5270	5280	5290
* * *	* * *	* * *	* * *	* * *	* * *	* * *
GTGAGGCACC	TATCTCAGCG	ATCTGTCTAT	TTCGTTCATC	CATAGTTGCC	TGACTCCCCG	TCGTGTAGAT
5300	5310	5320	5330	5340	5350	5360
* * *	* * *	* * *	* * *	* * *	* * *	* * *
AACTACGATA	CGGGAGGGCT	TACCATCTGG	CCCCAGTGCT	GCAATGATAC	CGCGAGACCC	ACGCTCACCG
5370	5380	5390	5400	5410	5420	5430
* * *	* * *	* * *	* * *	* * *	* * *	* * *
GCTCCAGATT	TATCAGCAAT	AAACCAGCCA	GCCGGAAGGG	CCGAGCGCAG	AAGTGGTCCT	GCAACTTTAT
5440	5450	5460	5470	5480	5490	5500
* * *	* * *	* * *	* * *	* * *	* * *	* * *
CCGCCTCCAT	CCAGTCTATT	AATTGTTGCC	GGGAAGCTAG	AGTAAGTAGT	TCGCCAGTTA	ATAGTTTGCG
5510	5520	5530	5540	5550	5560	5570
* * *	* * *	* * *	* * *	* * *	* * *	* * *
CAACGTTGTT	GCCATTGCTA	CAGGCATCGT	GGTGTCACGC	TCGTCGTTTG	GTATGGCTTC	ATTCAGCTCC
5580	5590	5600	5610	5620	5630	5640
* * *	* * *	* * *	* * *	* * *	* * *	* * *
GGTTCCCAAC	GATCAAGGCG	AGTTACATGA	TCCCCCATGT	TGTGCAAAAA	AGCGGTTAGC	TCCTTCGGTC
5650	5660	5670	5680	5690	5700	5710
* * *	* * *	* * *	* * *	* * *	* * *	* * *
CTCCGATCGT	TGTCAGAAGT	AAGTTGGCCG	CAGTGTTATC	ACTCATGGTT	ATGGCAGCAC	TGCATAATTC
5720	5730	5740	5750	5760	5770	5780
* * *	* * *	* * *	* * *	* * *	* * *	* * *
TCTTACTGTC	ATGCCATCCG	TAAGATGCTT	TTCTGTGACT	GGTGAGTACT	CAACCAAGTC	ATTCTGAGAA
5790	5800	5810	5820	5830	5840	5850
* * *	* * *	* * *	* * *	* * *	* * *	* * *
TAGTGTATGC	GGCGACCGAG	TTGCTCTTGC	CCGGCGTCAA	TACGGGATAA	TACCGCGCCA	CATAGCAGAA
5860	5870	5880	5890	5900	5910	5920
* * *	* * *	* * *	* * *	* * *	* * *	* * *

FIGURE 1F

CTTTAAAAGT GCTCATCATT GGAAAACGTT CTTCGGGGCG AAAACTCTCA AGGATCTTAC CGCTGTTGAG

5930 5940 5950 5960 5970 5980 5990

* * * * * * *

ATCCAGTTCG ATGTAACCCA CTCGTGCACC CAACTGATCT TCAGCATCTT TTACTTTCAC CAGCGTTTCT

6000 6010 6020 6030 6040 6050 6060

* * * * * * *

GGGTGAGCAA AAACAGGAAG GCAAAATGCC GCAAAAAGG GAATAAGGGC GACACGGAAA TGTGTAATAC

6070 6080 6090 6100 6110 6120 6130

* * * * * * *

TCATACTCTT CCTTTTTCAA TATTATTGAA GCATTTATCA GGGTTATTGT CTCATGAGCG GATACATATT

6140 6150 6160 6170 6180 6190 6200

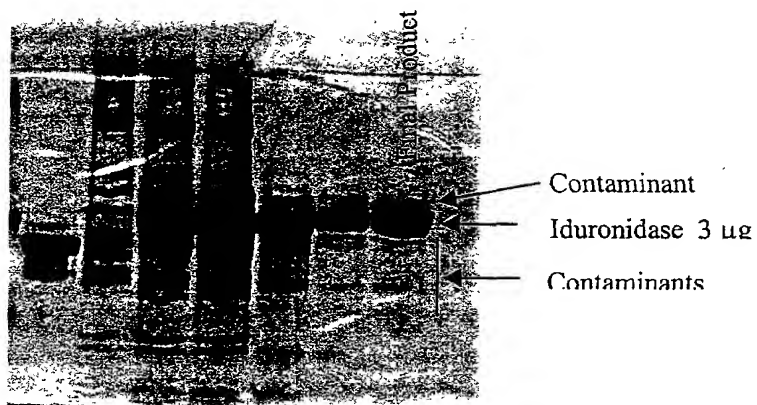
* * * * * * *

TGAATGTATT TAGAAAAATA AACAAATAGG GGTTCGCGC ACATTTCACC GAAAAGTGCC ACCTGACGTC

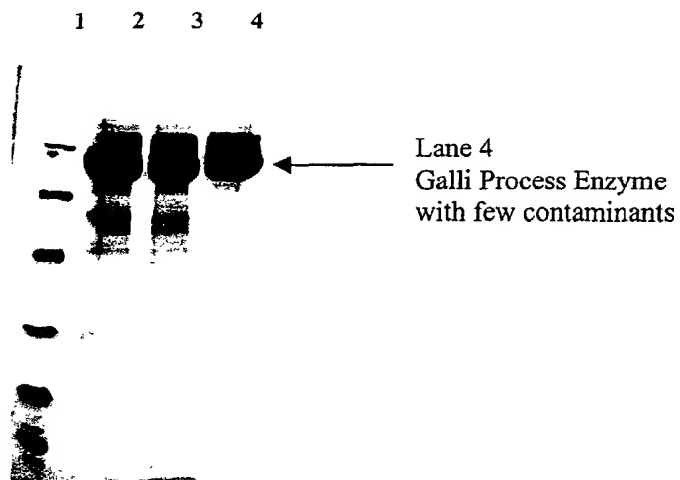
FIGURE 1G

FIGURE 2. SDS-POLYACRYLAMIDE GELS DEMONSTRATING IMPROVEMENTS IN PURITY

Gel using the Kakkis et al 1994, published procedure for purification



Gel using the new Galli Process contained in this application



1. Molecular Weight Marker
2. Prior Process Carson (nonpublished) Batch 2000C9001 Reference Reduced (7.5 μ g)
3. Same Batch 2000C9001 Reference Reduced (5.0 μ g)
4. Galli Process Enzyme Batch P10006 (5.0 μ g)

FIGURE 2

FIGURE 3A IDURONIDASE PRODUCTION USING THE GALLI PROCESS

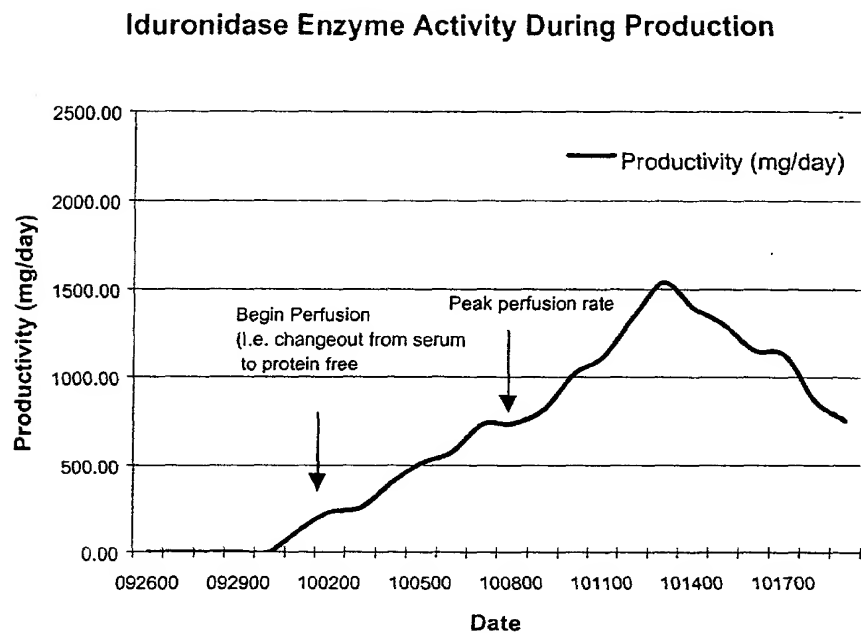
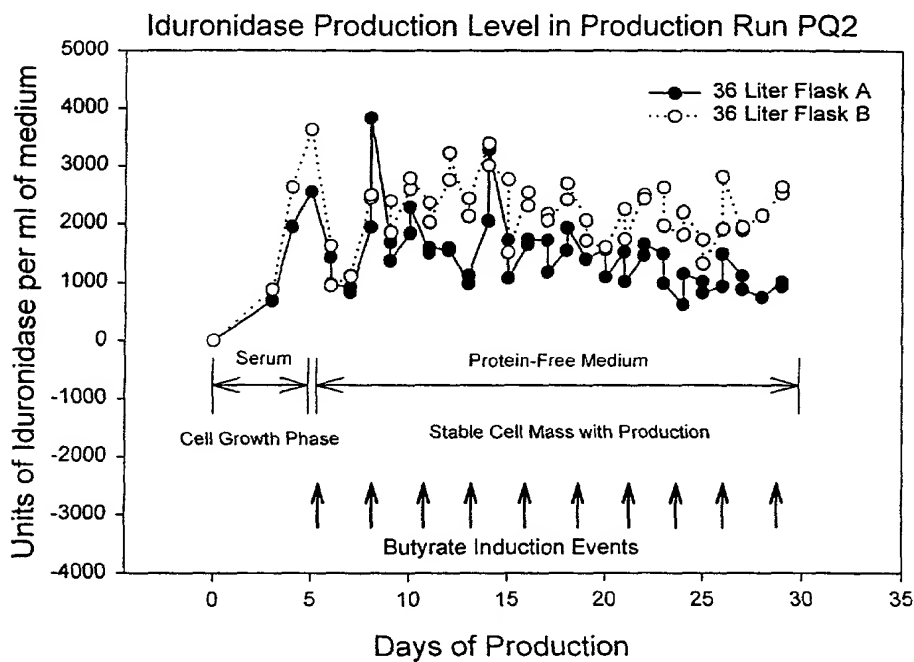


FIGURE 3B. IDURONIDASE PRODUCTION USING BUTYRATE INDUCTION



Reduction in Liver Volume During Enzyme Therapy

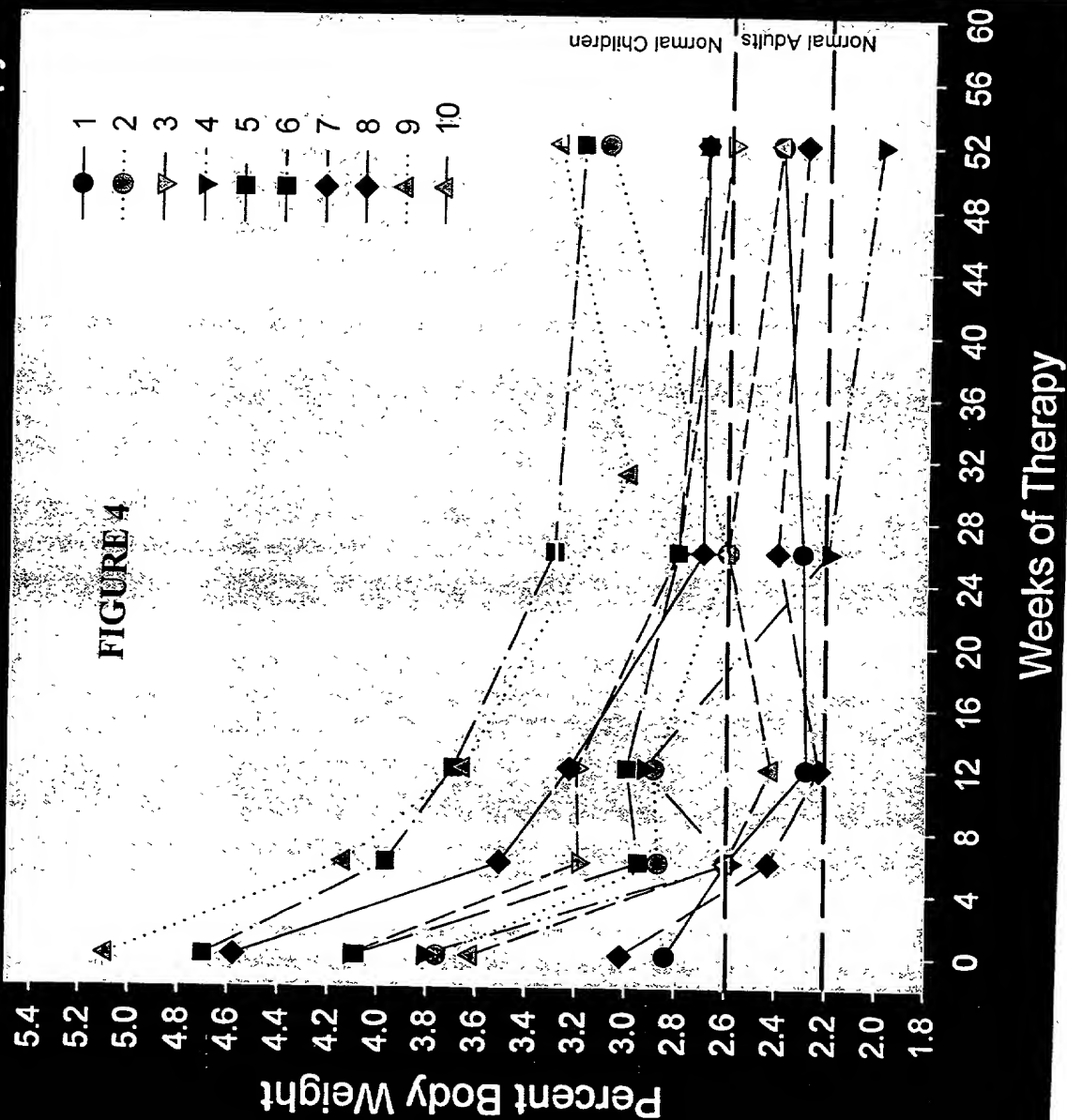


FIGURE 4

Urinary GAG Excretion During Enzyme Therapy

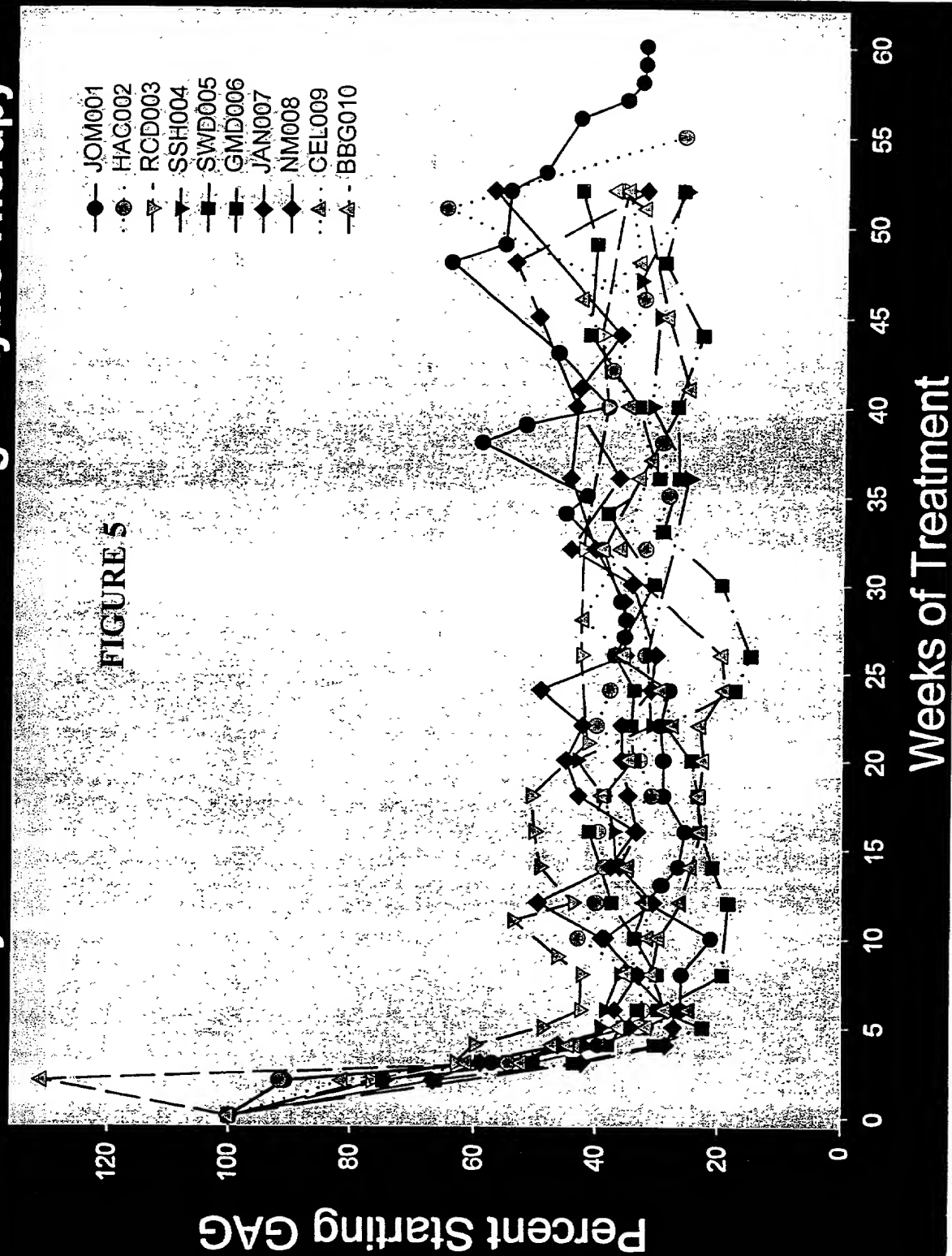


FIGURE 5

Elbow and Knee Extension in HAC002

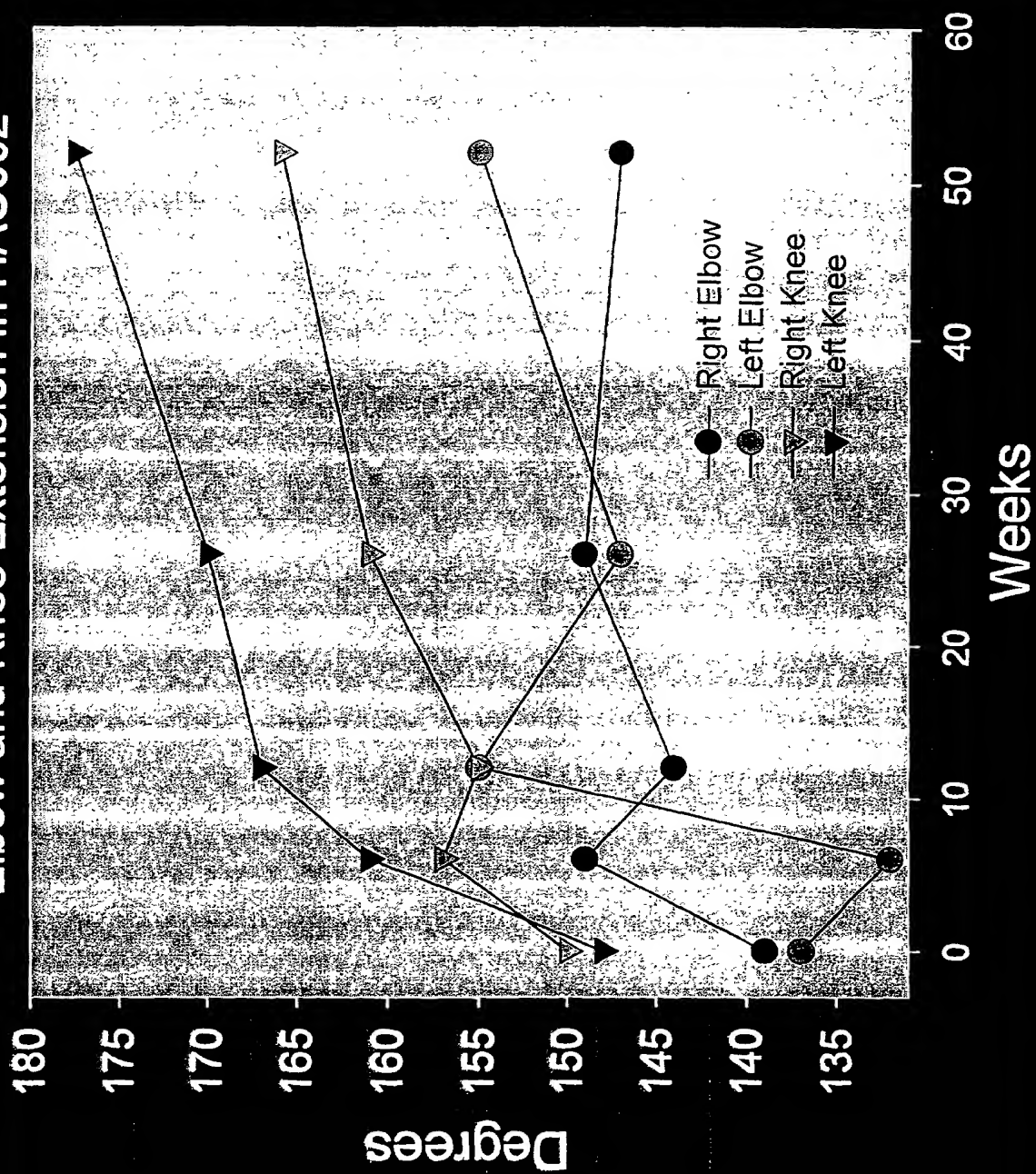


FIGURE 6

Shoulder flexion to 104 weeks in four patients with most restriction

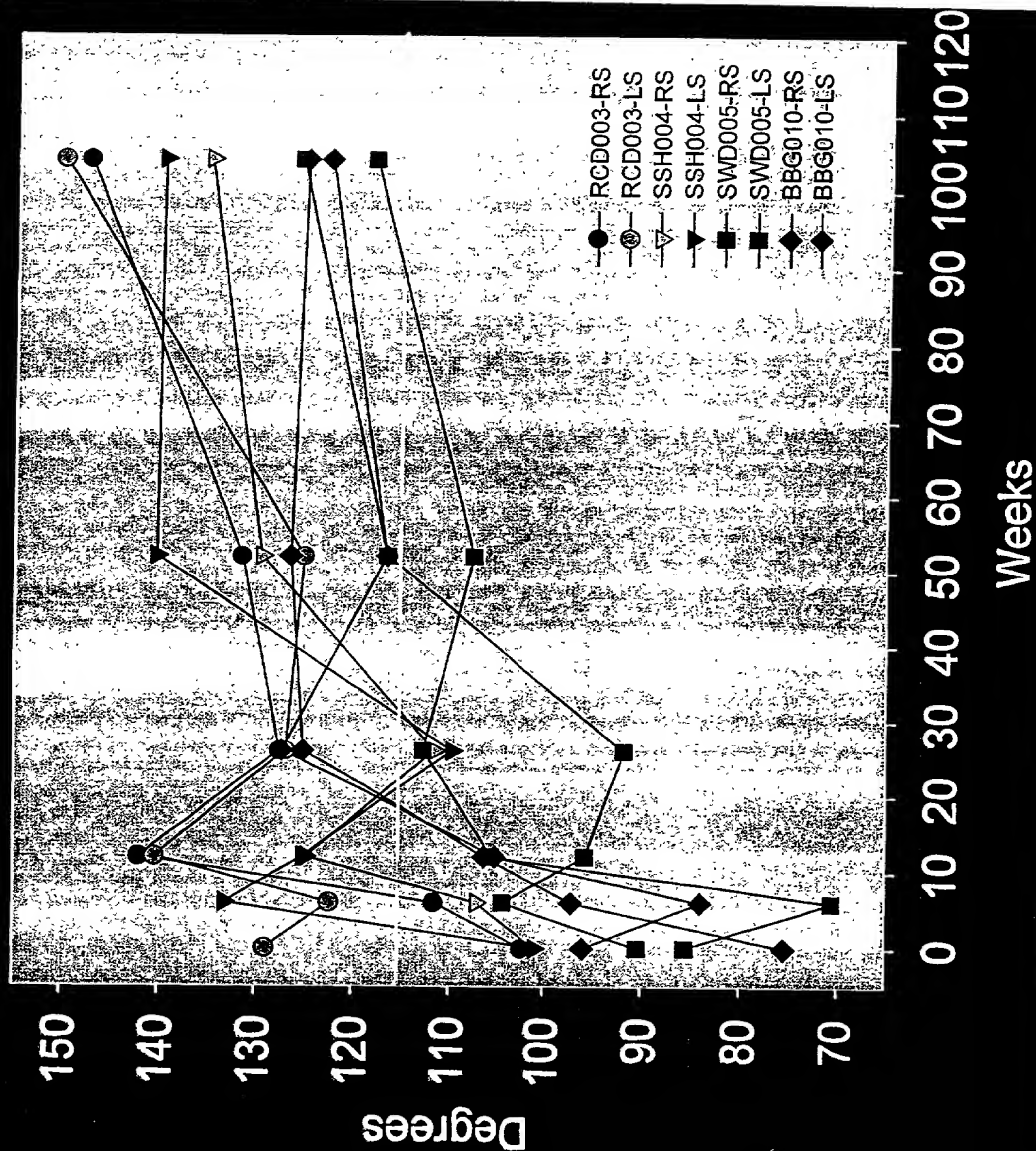
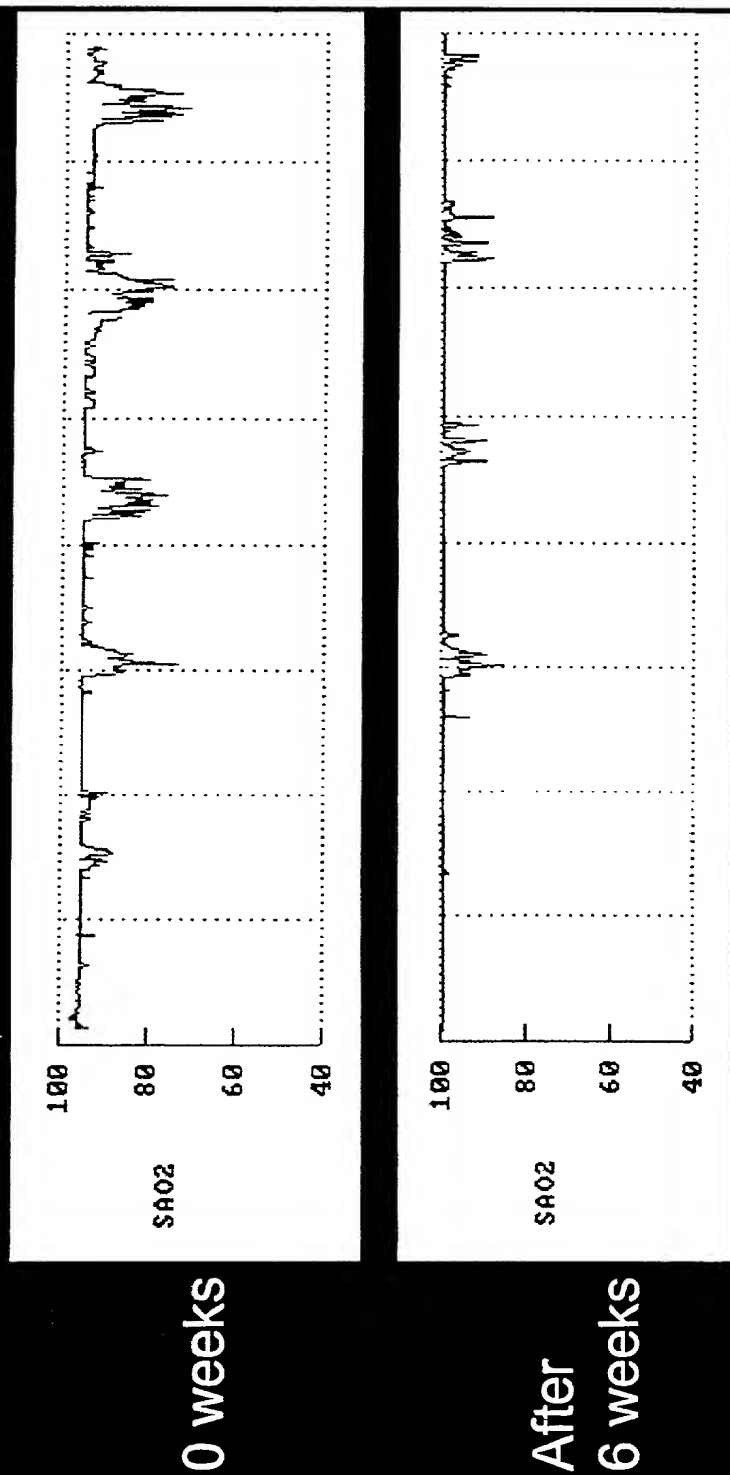


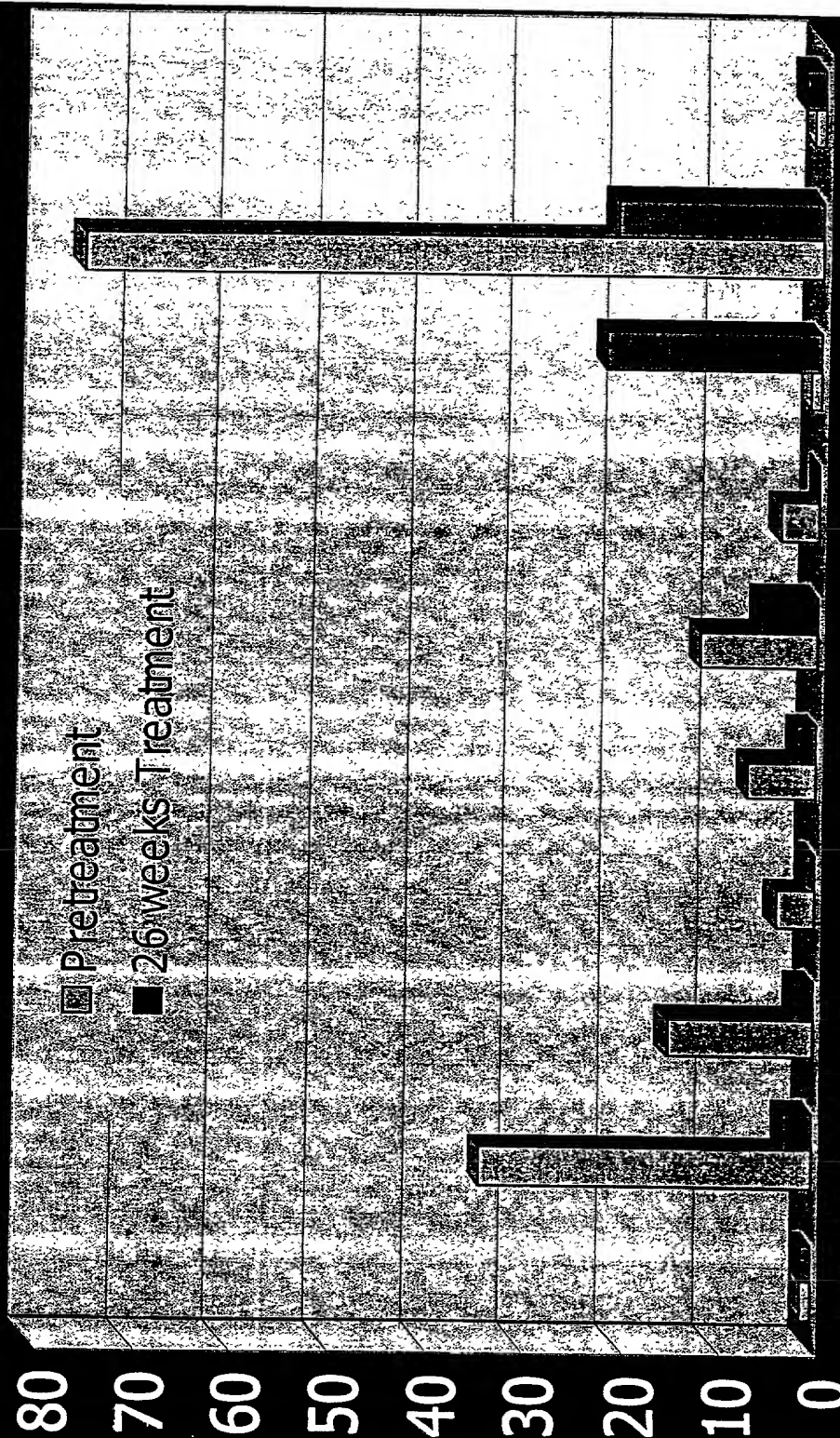
FIGURE 7

FIGURE 8

Sleep Apnea Improves



Apneas + Hypopneas During Sleep Pre and Post Treatment



JOM001 AHC002 RCD003 SSH004 SWD005 GMD006 JAN007 N-M008 CEL009 BBG010

FIGURE 9

Pulmonary Function Tests in GMD006

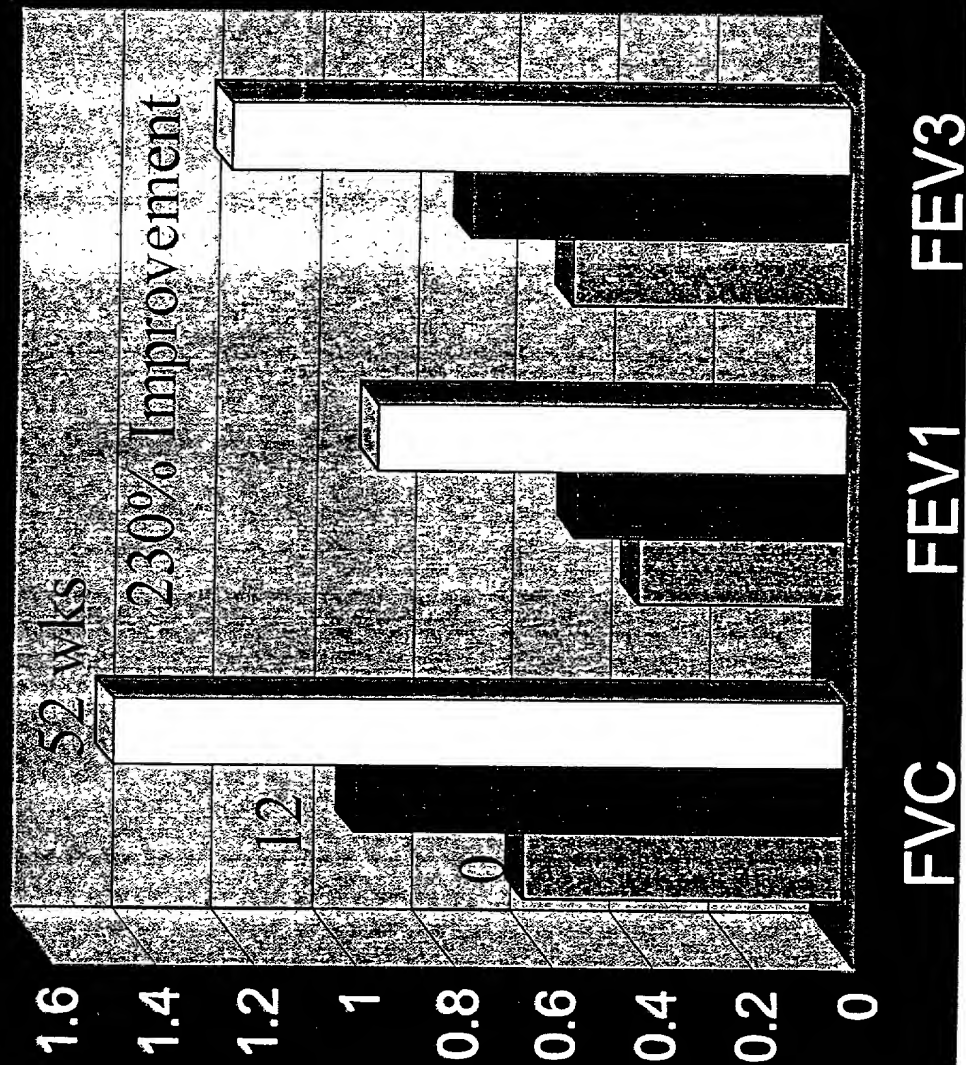


FIGURE 10

Increased Height Growth Velocity

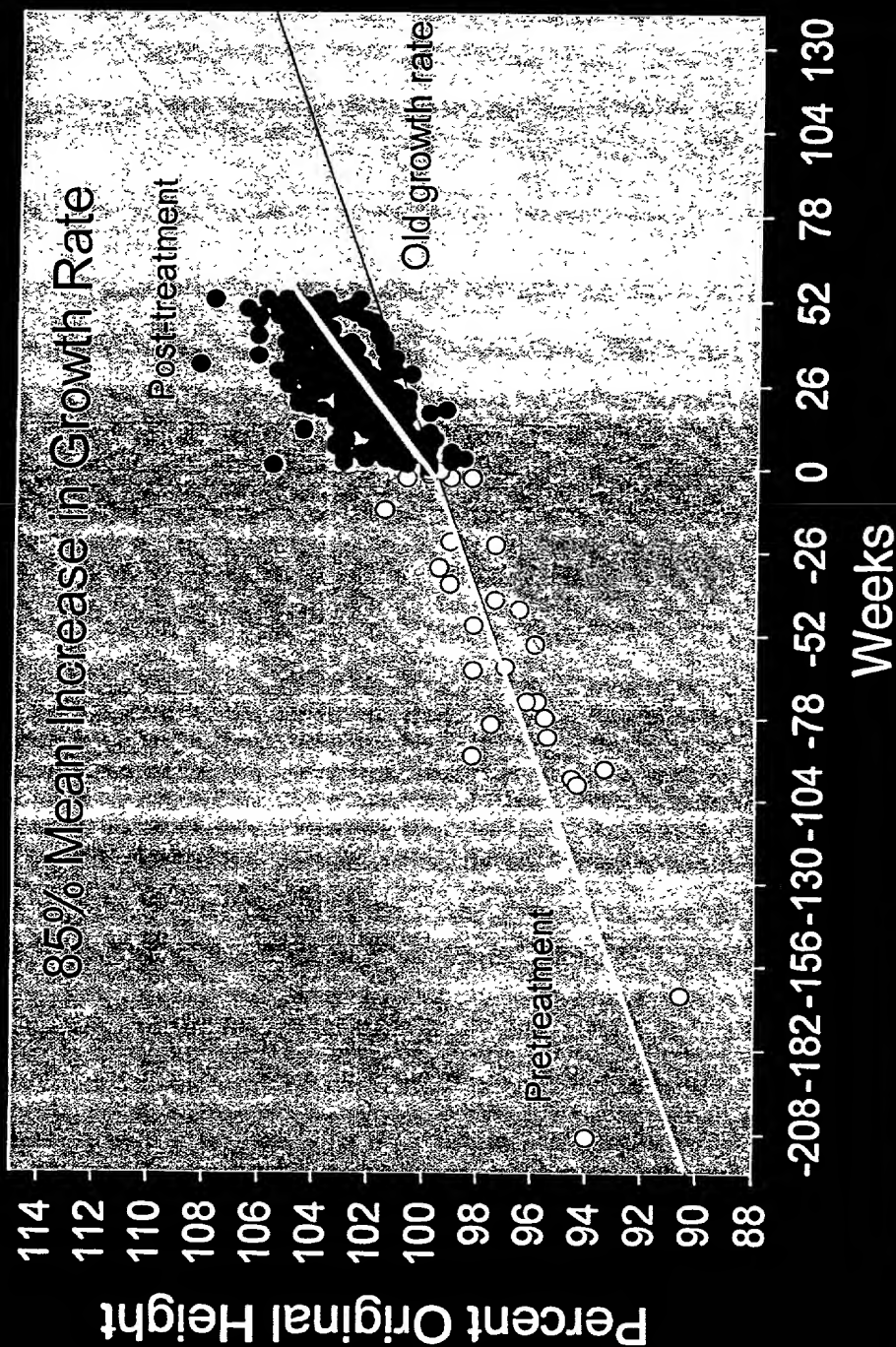


FIGURE 11

FIGURE 12.

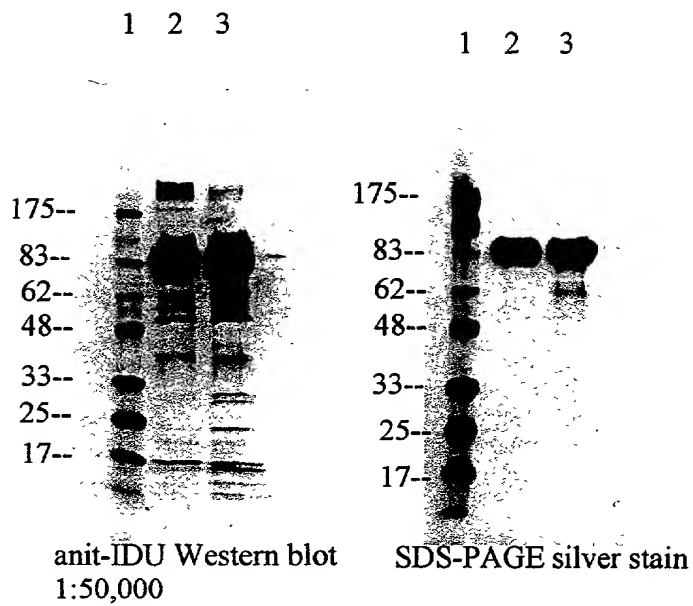
COMPARISON OF HOST PROTEIN CONTAMINATION BETWEEN A PRIOR AND THE NEW GALLI PROCESS

Chinese Hamster Ovary Host Protein Contamination by ELISA Assay

SOURCE AND BATCH NUMBER	CHOP PROTEIN CONTAMINATION (microgram per milligram)	PERCENT CHOP CONTAMINATION	PURITY OF THE ENZYME FROM CHOP
Prior Process (Carson/REI)			
C9002	14	1.4%	98.6%
C9003	24	2.4%	97.6%
C9004	16	1.6%	98.4%
New Process (Galli)			
P1003	<1.3	<0.13%	>99.9%
P1006	1.2	0.12%	99.9%
P1007	<0.6	<0.06%	>99.9%
P1008	<0.67	<0.067%	>99.9%

FIGURE 12

Comparison of Galli and Carson Material



- 1 Marker
- 2 Galli Referenced-0201
- 3 Carson C9002

5ug/lane

FIGURE 13